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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,439	09/11/2003	Takashi Okuda	242622US0X	4092
22850	7590	03/10/2004		
OBOLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314				
			EXAMINER	
			FIELD, TAMMY K	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,439	OKUDA ET AL.	
	Examiner	Art Unit	
	Tammy K. Field	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 11 September 2003.
2a) This action is **FINAL**. 2b) This action is non-final.
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-4 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-4 is/are rejected.

7) Claim(s) 3 and 4 is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 9/11/03.

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
5) Notice of Informal Patent Application (PTO-152)
6) Other: ____.

DETAILED ACTION

1. Claims 1-4 are presently under examination.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on March 17, 2003. It is noted that it appears applicants have not filed a translation of the certified copy of the Japanese application as required by 35 U.S.C. 119(a)-(d) and as such has been accorded the priority date of September 11, 2003 for prior art purposes.

Specification

3. The disclosure is objected to because of the following informalities:

- a. "P" should be spelled out the 1st time used in the specification at page 2.

Appropriate correction is required.

Claim Objections

4. Claims 3 and 4 are objected to because of the following informalities:
 - b. Claim 3 - "P." should be replaced with "Polypedilium" thereby being fully described when initially introduced in claim language.
 - c. Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The method of dry-preserving is not dependent on breeding of *Polypedium vanderplanki* as *P. vanderplanki* larva are immature forms and do not breed.

Information Disclosure Statement

The information disclosure statement filed on September 11, 2003 has been considered.

An initialed copy is enclosed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, and 3 and 4 as dependent from Claim 1 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a method of dry-preserving tissues of a multicellular organism of *Polypodium vanderplanki* by submerging the tissues in an insect fluid medium treated with heat and drying, does not reasonably provide enablement of a method for dry-preserving a tissue of a multicellular organism in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass a method for dry-preserving a tissue of a multicellular organism, comprising submerging the tissue of the multicellular organism in an insect fluid medium treated with heat, and drying for 48 hours, wherein the multicellular organism is *Polypodium vanderplanki*.

The teachings of the specification are limited to the breeding of *P. vanderplanki* and dry-preserving the tissues of larva of *P. vanderplanki* comprising submerging the tissue an insect fluid medium, treated with heat, and drying in a desiccator for 24 hr or more.

The teachings of the specification are silent regarding working examples of any other tissue of a multicellular organism, *i.e.* animals (*e.g.* Humans), plants, and/or other insects in a method for dry-preserving tissues. The specification is also silent regarding any limitations of tissue size relating to the infusion of insect body fluid medium in the instant dry-preserving method. Is applicant able to dry-preserve a tissue such as a pint of whole blood, the frontal lobe of a human brain, or other types of mammalian tissues such as lymphatic, pancreatic, and/or cardiac? The specification is additionally silent to any relationship the instant method shares with plants that are made of different types of tissues and/or do not contain the organ tissues of a fat body or liver, muscle, and/or gastrointestinal tract. The specification is also silent to how other environmental factors are regulated, *e.g.* oxygen content during initial drying of a multicellular organism and/or the presence of free radicals that could inherently affect dry-preserving conditions, as well as storage factors upon dry-preserving with different tissues of a multicellular organism. Further, do other tissues produce substances, *e.g.* trehalose in response to lack of water and/or oxygen? Are there other tissues that contain cells which have inducible expression of trehalose that appear to be important in the dry-preserving of tissues? How does submerging the tissue in insect body fluid affect the dry-preserving of multicellular organisms of other insects, animals, and/or plants?

Gordon, S.L. *et al.* September 2001 (Cryobiology 43(2): 182-187) teach preliminary findings of human mesenchymal stem cells (hMSCs) dry-preserved using trehalose compared to

controls that do not recover in the absence of trehalose at Materials and Methods, page 183.

Gordon, S.L. *et al.* further teach trehalose has broad potential uses in tissue engineering and regeneration indicative of differentiation potential for fat and bone (see abstract). Gordon, S.L. *et al.* conclude that although preliminary findings are encouraging, research addressing consistency and duration of storage by considering factors such as cell water content, oxygen concentration, and the presence of free radicals still need to be addressed (see Discussion, pages 186-187).

In view of the state of the prior art set forth *supra* and/or full scope of Applicant's claimed invention, it would require undue experimentation by one of ordinary skill in the art to practice the claimed invention in the tissues of other insects, plants, and animals such as humans. Due to the level of predictability, without working examples and further direction provided by the inventor demonstrating dry-preserving of other insect, plant and/or animal tissues, one of ordinary skill in the art would be unable to apply a method of dry-preserving of *P. vanderplanki* tissue directly to other insect, plant, or animal tissue. Since the office does not have the facilities for examining applicants' scope of invention specifically related to a method for dry-preserving a tissue of multicellular organisms effective for other insects, plants and animals such as Humans, the burden is on the Applicant(s) to provide evidence of why the claimed method is enabled. At present examination, Applicants have not presented sufficient evidence to practice the claimed invention.

6. Claims 2, 3 and 4 as dependent from claim 2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of dry-preserving tissues of a larva of *Polypedium vanderplanki* by placing a drying container containing a larva of a

multicellular organism in a desiccator, does not reasonably provide enablement for a method for dry-preserving a tissue of a multicellular organism as many multicellular organisms do not contain a larval stage of growth. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass a method for dry-preserving a tissue of a multicellular organism comprising placing a drying container containing a larva of a multicellular organism in a desiccator (humidity < 5% and evaporating distilled water in drying container of 220-230 μ l/24hr), wherein the multicellular organism is *Polypodium vanderplanki*.

The teachings of the specification are limited to the breeding of *P. vanderplanki* and dry-preserving the larval forms of *P. vanderplanki* by placing a group of ten larvae in a drying container containing distilled water and filter paper and placing in a desiccator (humidity < 5% and evaporating distilled water in drying container of 220-230 μ l/24hr).

The teachings of the specification are silent regarding working examples of any other tissues from other larvae of multicellular organisms, *i.e.* animals (*e.g.* roundworms), plants, and/or other insects in the instant method for dry-preserving tissues. The specification is also silent regarding any limitations of tissue size of larva relating to the instant dry-preserving method. How does applicant get the insect body fluid medium inside deeply embedded cells within tissues of a larger multicellular organism? Is applicant able to dry-preserve other multicellular organisms that do not have a larval stage, *i.e.* plants or animals such as humans? The specification mentions tissue responses to dehydration stress of plants without providing collaborating evidence directly relating self containing anhydrobiosis to the instant method.

What does applicant mean by anhydrobiosis? What are the mechanisms involved in dry-preserving and/or cryptobiosis of tissues in a multicellular organism and their relation to applicants claimed method? Are there other tissues that contain cells that have inducible expression of trehalose which appear to be important in the dry-preserving of tissues in a multicellular organism? How does having inducible expression of trehalose in cells affect the instant dry-preserving method in multicellular organisms of other insects, animals, and/or plants?

The teachings of Schwarz, K. (Un. of Florida Book of Insect Records, Chapter 5 © 1994, Gainesville, FL.) clearly state that *Polypodium vanderplanki* is the only insect known to endure the cryptobiotic state and survive dehydration to a moisture content of < 3% (see Results). Schwarz, K. further teach since virtually all insects are not capable of entering the cryptobiotic state further investigation is needed to confirm whether these or other insects can enter cryptobiosis (see Discussion). This lends significant weight to then question if any insect other than *Polypodium vanderplanki* is appropriate to use in Applicant's claimed invention.

Watanabe, M. *et al.* 2002. (J. Exper. Bio. 205: 2799-2802) teach the underlying molecular and metabolic mechanisms of cryptobiosis largely remain a mystery (see Introduction, paragraph 2). Watanabe, M. *et al.* further teach rapid accumulation of trehalose plays a key role in the successful induction of cryptobiosis in *P. vanderplanki* (see Table 1). Watanabe, M. *et al.* suggest further investigations are needed to elucidate the mechanism(s) of the successful induction and recovery of cryptobiosis in the "higher" invertebrate *P. vanderplanki* and might be of enormous consequence for the field of cell and organ storage (see page 2801 at Table 1 and Discussion, paragraph 4). Applicants have not demonstrated any tissues (other than *P.*

vanderplanki) that can undergo the rapid accumulation of trehalose that appears key to a successful induction of cryptobiosis.

In view of the state of the prior art set forth *supra* and/or full scope of Applicant's claimed invention, it would require undue experimentation by one of ordinary skill in the art to practice the claimed invention in the tissues of other insects, plants, and animals such as humans. Due to the level of predictability, without working examples and further direction provided by the inventor demonstrating dry-preserving of other insect, plant and/or animal tissues, one of ordinary skill in the art would be unable to apply a method of dry-preserving of *P. vanderplanki* tissue directly to other insect, plant, or animal tissue. Since the office does not have the facilities for examining applicants' scope of invention specifically related to a method for dry-preserving a tissue of multicellular organism effective for other insects, plants and animals such as Humans, the burden is on the Applicant(s) to provide evidence of why the claimed method is enabled. At present examination, Applicants have not presented sufficient evidence to practice the claimed invention.

7. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims and bounds of the claimed subject matter. The claims are indefinite in the recitation of "evaporating distilled water in the drying container" because it is unclear from the specification what applicant intends. The method of dry-preserving is not dependent on the breeding of *P. vanderplanki*.

Clarification is required in order to overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 2 - 4 rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Watanabe, M. *et al.* Nov. 2002. (J. Exp. Bio. 205: 2799-2802).

The claims are drawn to a method for dry-preserving a tissue of a multicellular organism comprising submerging the tissue in an insect fluid medium treated with heat, and drying in a desiccator for 24 hr or more. Subsequent claims read on a method for dry-preserving a larva of a multicellular organism in a desiccator (humidity < 5% and evaporation rate of 220 to 230 μ l/24hr), wherein the multicellular organism is *Polypodium vanderplanki*.

Watanabe, *et al.* teach a method for dry-preserving larva (*i.e.* larva contain tissues) of *P. vanderplanki* using a desiccator (<5% relative humidity) and drying over a period of 48h (0.22-0.23 ml/dy⁻¹ (*i.e.* 220 to 230 μ l/24hr) in Material and Methods, Desiccating Procedure page 2799.

As to claim 4, the claim recites wherein the *P. vanderplanki* is bred at a specific humidity etc., however claim 2 from which this claim depends uses larva and therefore is unclear how this step provides for larva and adds to the claimed method for dry presenting a larva as required by claim 2. For purposes of this art rejection, this limitation has been interpreted as a method of obtaining the larva of claim 2 by breeding *P. vanderplanki*. Watanabe, *et al.* teaches a method of breeding *P. vanderplanki* in order to obtain larva for dry-preserving. The method of Watanabe,

et al. teaches breeding of cryptobiotic larvae of *P. vanderplanki*, by transferring larvae into a plastic container containing water on autoclaved soil and aerated continuously. The larvae were reared for successive generations under controlled light (13h:11h light:dark) and temperature 27°C. While the reference does not specifically teach the humidity levels, since the breeding took place in a chamber with water and in the absence of evidence to the contrary, the water and temperature inherently produce the condition of humidity levels of 80%. As such, the method of breeding does not appear to provide any distinguishing feature of the larva that is used in the method of dry preservation, nor is it distinguished from the method of the prior art. As such, the breeding of the *P. vanderplanki* by the method of the prior art is inherently the same as claimed.

Thus, Watanabe, *et al.* anticipates the instantly claimed invention.

9. Since the office does not have the facilities for examining and comparing applicants' methods with the methods disclosed in the prior art, the burden is on applicants to show a novel or unobvious difference between the claimed methods and the methods of the prior art (*i.e.* that the methods of the prior art does not possess the same material structural and functional characteristics of the claimed methods).

Status of the Claims

10. No claims allowed.

Conclusion

11. The prior art of record and not relied upon is considered pertinent to applicant's disclosure:

- a. Crowe, J. *et al.* 1986. (*in* Metabolism and Dry Organisms, Chapter 11, "Stabilization of membranes in anhydrobiotic organisms", Comstock Publishing, pages 188-209).
- d. Crowe, J. *et al.* 1988. Biochem. Biophys. Acta 947: 367-384.

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- e. Colaco, C *et al.* (US Pat. 6,313,102 published November 6, 2001).
- f. Guo, N. *et al.* 2000. (Nat. Biotechnol. 18 :168-171).
- g. Puhlev, I. *et al.* 2001. (Cryobiology 42 : 207-217).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tammy K. Field whose telephone number is (571) 272-0856. The examiner can normally be reached on Monday-Friday from 7am-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (571) 272- 0864.

Papers relating to this application may be submitted to Technology Center 1600 Group 1640 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and After Final communications.



Tammy K. Field
March 7, 2004

Patricia A. Duffy
PATRICIA A. DUFFY
PRIMARY EXAMINER